

What is Claimed is:

1. A method for inducing infertility in an animal comprising inhibiting SMC1 β expression or activity in said animal.
2. The method of claim 1, wherein said inhibiting comprises contacting
5 said animal with a nucleic acid selected from the group consisting of a nucleic acid that is an antisense SMC1 β nucleic acid and a compound 8 to 80 nucleotides in length targeted to a nucleic acid molecule encoding SMC1 β , wherein said compound specifically hybridizes with a nucleic acid molecule of SEQ ID NO: 1 or 3 and inhibits the expression of SMC1 β .
3. The compound of claim 2 comprising 12 to 50 nucleotides in length.
- 10 4. The compound of claim 2 comprising 15 to 30 nucleotides in length.
5. The compound of claim 2 comprising 20 to 25 nucleotides in length.
6. The compound of claim 3 wherein said compound is an antisense oligonucleotide.
- 15 7. The compound of claim 6 wherein said compound is a DNA oligonucleotide.
8. The compound of claim 6 wherein said compound is an RNA oligonucleotide.
9. The compound of claim 4 wherein at least a portion of said compound hybridizes with RNA to form an oligonucleotide-RNA duplex.
- 20 10. A method for inducing infertility in an animal, comprising administering to an animal an effective contraceptive amount of an agent that inhibits SMC1 β expression or activity.
11. The method of claim 10 which further comprises restoring fertility to said animal by ceasing administration of said agent.
- 25 12. The method of claim 10, wherein said infertility is caused by blocking spermatogenesis.
13. The method of claim 12, wherein said spermatogenesis is blocked by inhibiting meiosis.
14. The method of claim 10, wherein said infertility is caused by blocking
30 oogenesis.

15. The method of claim 14, wherein said oogenesis is blocked by inhibiting meiosis.

16. The method of claims 13 or 15, wherein said meiosis is inhibited at prophase of meiosis I or later.

5 17. The method of any of claims 10 through 16, wherein said agent is selected from the group consisting of: a nucleic acid construct, a small molecule antagonist of SMC1 β , a peptidomimetic antagonist of SMC1 β , and an anti-SMC1 β antibody.

18. The method of claim 17, wherein the agent is administered in a composition comprising a pharmaceutically acceptable carrier.

10 19. The composition of claim 18, wherein the pharmaceutically acceptable carrier is an adjuvant, solubilizer, stabilizer, diluent, anti-oxidant, liposome, micelle, or patch.

20. A method of treating infertility in an animal, comprising administering to said animal an effective therapeutic amount of exogenous SMC1 β or an agent that induces SMC1 β expression or activity.

15 21. The method of claim 20, wherein said infertility is treated by stimulating spermatogenesis.

22. The method of claim 21, wherein said spermatogenesis is stimulated by inducing meiosis.

20 23. The method of claim 20, wherein said infertility is treated by stimulating oogenesis.

24. The method of claim 23, wherein said oogenesis is stimulated by inducing meiosis.

25 25. The method of claims 22 or 24, wherein said meiosis is induced at or after prophase of meiosis I.

26. The method of any of claims 20 through 25, wherein said agent is selected from the group consisting of: a nucleic acid construct that encodes the SMC1 β polypeptide, a SMC1 β polypeptide, a small molecule agonist of SMC1 β , and a peptidomimetic agonist of SMC1 β .

30 27. The method of claim 26, wherein the agent is administered in a composition comprising a pharmaceutically acceptable carrier.

28. The composition of claim 27, wherein the pharmaceutically acceptable carrier is an adjuvant, solubilizer, stabilizer, diluent, anti-oxidant, liposome, micelle, or patch.

29. The method of claims 18 or 27, wherein the agent is administered orally, parenterally, topically, transdermally, systemically, intravenously, intraarterially,
5 intraperitoneally, or intramuscularly.

30. The method of claims 12 or 21, wherein the administration is to the testis.

31. The method of claim 30, wherein the administration to the testis is by a route selected from the group consisting of: injection, implantation, and transdermal
10 application.

32. The method of claims 5 or 14, wherein the administration is to the ovary.

33. The method of claim 23, wherein the administration is by injection or implantation into the ovary.

34. The method of claims 10 or 20, wherein the animal is human.

35. A method of inhibiting meiosis in germ cells, comprising inhibiting the expression or activity of SMC1 β in said cells.

36. The method of claim 35, wherein said germ cells are spermatocytes.

37. The method of claim 35, wherein said germ cells are oocytes.

38. The method of claim 35, wherein said meiosis is inhibited at prophase
20 of meiosis I.

39. The method of claim 38, wherein said cells are treated *in vitro*.

40. The method of claim 38, wherein said cells are treated *in vivo*.

41. The method of claim 38, wherein said cells are treated in an animal
25 subject.

42. The method of claim 41, wherein said subject is human.

43. The method of claim 35, wherein said method comprises contacting said cells with an agent that reduces the expression or activity of SMC1 β .

44. The method of claim 43, wherein said agent is a nucleic acid construct.

45. The method of claim 43, wherein said agent is a small molecule antagonist of SMC1 β .

46. The method of claim 43, wherein said agent is a peptidomimetic antagonist of SMC1 β .

5 47. The method of claim 43, wherein said agent is an anti-SMC1 β antibody.

48. The method of any of claims 43 through 47, wherein the agent is administered in a composition comprising a pharmaceutically acceptable carrier.

10 49. The method of claim 48, wherein the pharmaceutically acceptable carrier is an adjuvant, solubilizer, stabilizer, diluent, anti-oxidant, liposome, micelle, or patch.

50. A method of inducing meiosis in germ cells, comprising inducing the expression or activity of SMC1 β in said cells.

51. The method of claim 50, wherein said germ cells are spermatocytes.

52. The method of claim 50, wherein said germ cells are oocytes.

15 53. The method of claim 50, wherein said meiosis is induced at prophase of meiosis I.

54. The method of claim 50, wherein said cells are treated *in vitro*.

55. The method of claim 50, wherein said cells are treated *in vivo*.

20 56. The method of claim 55, wherein said cells are treated in an animal subject.

57. The method of claim 56, wherein said subject is human.

58. The method of claim 50, wherein said method comprises contacting said cells with exogenous SMC1 β or an agent that induces the expression or activity of SMC1 β .

25 59. The method of claim 58, wherein said agent is a nucleic acid construct that encodes an SMC1 β polypeptide.

60. The method of claim 58, wherein said agent is an SMC1 β polypeptide.

61. The method of claim 58, wherein said agent is a small molecule agonist of SMC1 β .

62. The method of claim 58, wherein said agent is a peptidomimetic agonist of SMC1 β .

5 63. The method of any of claims 58 through 62, wherein the agent is administered in a composition comprising a pharmaceutically acceptable carrier.

64. The method of claim 63, wherein the pharmaceutically acceptable carrier is an adjuvant, solubilizer, stabilizer, diluent, anti-oxidant, liposome, micelle, or patch.

10 65. A method for treating a disorder in an animal resulting from decreased levels of SMC1 β polypeptide comprising administering to an animal an SMC1 β polypeptide or the nucleic acid encoding the polypeptide of SMC1 β to said animal.

66. A method of diagnosing a disorder or susceptibility to a disorder in an animal caused by or resulting from abnormal levels of SMC1 β polypeptide comprising:

15 a) determining the presence or amount of expression or activity of an SMC1 β polypeptide or a nucleic acid encoding the polypeptide of SMC1 β in a sample; and

b) comparing the level of SMC1 β polypeptide or the nucleic acid encoding the polypeptide of SMC1 β in a biological, tissue, or cellular sample from normal animals or the animal at an earlier time, wherein the presence or susceptibility to the disorder is based on the presence or amount of expression or activity of the SMC1 β polypeptide or the nucleic acid
20 encoding the polypeptide of SMC1 β .

67. The method of any one of claims 65 or 66, wherein the disorder is selected from the group consisting of infertility, a pathological condition, and a nondisjunction syndrome.

25 68. A composition comprising exogenous SMC1 β or an agent that induces SMC1 β expression or activity and a pharmaceutically acceptable carrier.

69. The composition of claim 68, wherein said agent is selected from the group consisting of a nucleic acid construct that encodes SMC1 β polypeptide, an SMC1 β polypeptide, a small molecule agonist of SMC1 β , and a SMC1 β peptidomimetic agonist.

70. A composition comprising an agent that reduces SMC1 β expression or activity and a pharmaceutically acceptable carrier.

71. The composition of claim 70, wherein said agent is selected from the group consisting of a nucleic acid construct that encodes SMC1 β in an antisense orientation, a selective binding agent of SMC1 β polypeptide, a small molecule antagonist of SMC1 β , and an SMC1 β peptidomimetic antagonist.

72. The composition of any one of claims 68 or 70, wherein the pharmaceutically acceptable carrier is an adjuvant, solubilizer, stabilizer, diluent, anti-oxidant, liposome, micelle, or patch.

73. The composition of claim 69, wherein said polynucleotide is contained within a vector.

74. A diagnostic reagent comprising a detectably labeled polynucleotide encoding the SMC1 β polypeptide, or a fragment, variant or homolog thereof.

75. The diagnostic reagent of claim 74, wherein said labeled polynucleotide is a first-strand cDNA.

76. A method for detecting the presence of an SMC1 β nucleic acid in a biological sample comprising the steps of:

- a) providing a biological sample suspected of containing an SMC1 β nucleic acid;
- b) contacting the biological sample with a diagnostic reagent according to claim 74 under conditions, wherein the diagnostic reagent will hybridize with an SMC1 β nucleic acid;
- c) detecting hybridization between an SMC1 β nucleic acid in the biological sample and the diagnostic reagent; and
- d) comparing the level of hybridization between the biological sample and diagnostic reagent with the level of hybridization between a known concentration of an SMC1 β nucleic acid and the diagnostic reagent, thereby detecting the presence of an SMC1 β nucleic acid in the sample.

77. The method of claim 76, wherein said nucleic acid is DNA.

78. The method of claim 76, wherein said nucleic acid is RNA.

79. A method for screening agents that modulate meiosis in germ cells comprising:

- a) providing a cell expressing SMC1 β ;
- b) contacting said cell with a candidate modulating agent;
- 5 c) monitoring said cell for a change in meiotic activity in the presence and absence of the candidate modulating agent; and
- d) identifying a candidate modulating agent as a modulating agent when the meiotic activity differs in the presence or absence of the agent.

10 80. The method of claim 79, wherein said modulating agent increases meiosis.

81. The method of claim 79, wherein said modulating agent decreases meiosis.

82. The method of claim 79, wherein said cell is a spermatocyte.

83. The method of claim 79, wherein said cell is an oocyte.

15 84. The method of claim 79, wherein said cell is from a transgenic, non-human animal.

85. The method of claim 79, wherein said contacting is performed *in vitro*.

86. The method of claim 79, wherein said contacting is performed *in vivo*.

20 87. The method of claim 79, wherein said candidate modulating agent is a nucleic acid construct that reduces the expression or activity of SMC1 β .

88. The method of claim 79, wherein said candidate modulating agent is a nucleic acid construct that increases the expression or activity of SMC1 β .

89. The method of claim 79, wherein said candidate modulating agent is an antibody of SMC1 β .

25 90. The method of claim 79, wherein said candidate modulating agent is a small molecule antagonist of SMC1 β .

91. The method of claim 79, wherein said candidate modulating agent is a peptidomimetic antagonist of SMC1 β .

92. A composition comprising a candidate modulating agent of meiosis identified according to the method of any of claims 80 through 91 and a pharmaceutically acceptable carrier.

93. The composition of claim 92, wherein the pharmaceutically acceptable carrier is an adjuvant, solubilizer, stabilizer, diluent, anti-oxidant, liposome, micelle, or patch.

94. A method of modulating SMC1 β activity in a cell of an animal comprising administering to the animal the composition of claim 93.

95. A method of modulating meiosis in an animal comprising administering to the animal the composition of claim 93.

96. A method for identifying agents that modulate SMC1 β expression or activity in a germ cell comprising:

- a) providing a cell expressing SMC1 β ;
- b) contacting said cell with a candidate modulating agent;
- c) monitoring said cell for a change in SMC1 β expression or activity in the presence and absence of modulating agent; and
- d) identifying a candidate modulating agent as a modulating agent when SMC1 β expression or activity differs in the presence or absence of the agent.

97. A method for identifying agents that inhibit SMC1 β expression or activity in germ cells comprising:

- a) introducing an inducible expression construct of SMC1 β into a somatic cell;
- b) contacting said cell with a candidate inhibitor of SMC1 β ; and
- c) monitoring said cell for an increase in proliferation;

wherein an increase in cell proliferation identifies the agent as an SMC1 β inhibiting agent.

98. A composition comprising the candidate modulating agent of meiosis or SMC1 β expression or activity identified according to the method of claim 96 and a pharmaceutically acceptable carrier.

99. A composition comprising the candidate inhibiting agent of meiosis or SMC1 β expression or activity identified according to the method of claim 97 and a pharmaceutically acceptable carrier.

100. The composition of any one of claims 98 or 99, wherein the pharmaceutically acceptable carrier is an adjuvant, solubilizer, stabilizer, diluent, anti-oxidant, liposome, micelle, or patch.

101. A method of modulating SMC1 β activity in an animal comprising administering to the animal the composition of any one of claims 98 or 99.

102. A method of modulating meiosis in an animal comprising administering to the animal the composition any one of claims 98 or 99.

103. A transgenic non-human animal whose genome comprises a homozygous null mutation in the endogenous SMC1 β gene, wherein said non-human animal exhibits abnormal development of a germ cell.

104. An isolated cell from a transgenic non-human animal whose genome comprises a homozygous null mutation in the endogenous SMC1 β gene, wherein production of functional SMC1 β is inhibited.

105. The cell of claim 103, wherein the cell is a mouse cell.

106. A method of evaluating a fertility treatment, comprising:

a) administering said treatment to a transgenic mouse whose genome comprises a homozygous null mutation in the endogenous SMC1 β gene, wherein said mouse exhibits abnormal development of the germ cells and is infertile; and

b) determining the effect of the treatment on the fertility of said mouse, thereby evaluating said fertility treatment.

107. The method of claim 106, wherein said treatment is evaluated *in vivo*.

108. The method of claim 106, wherein said treatment is evaluated *in vitro*.

109. The method of claim 106, wherein the effect of the treatment is determined by sperm count.

110. The method of claim 106, wherein the effect of the treatment is determined by testicular size.

111. The method of claim 106, wherein the effect of the treatment is determined by gamete morphology.

112. The method of claim 111, wherein the gamete is an oocyte.

113. The method of claim 111, wherein the gamete is a sperm cell.

5 114. The method of claim 106, wherein the effect of the treatment is determined by chromosome morphology.

115. The method of claim 106, wherein the effect of the treatment is determined by the ability of chromosomes to pair.

10 116. The method of claim 106, wherein the effect of the treatment is determined by the ability of the mice to mate and produce offspring.

117. The method of claim 106, wherein the effect of the treatment is determined by the ability of the mice to have normal estrous cycles.

118. The method of claim 106, wherein the effect of the treatment is determined by ovarian morphology.

15 119. An expression construct comprising a nucleic acid encoding a SMC1 β polypeptide, fragment, or variant thereof and a heterologous germ cell-specific promoter operably linked to said construct.

120. The construct of claim 119, wherein the nucleic acid is in a sense orientation with respect to the promoter.

20 121. The construct of claim 119, wherein the nucleic acid is in an antisense orientation with respect to the promoter.

122. The construct of claim 119, which is contained within a viral vector.

123. The construct of claim 119, wherein said promoter is a testis-specific promoter.

25 124. The construct of claim 123, wherein said promoter is the promoter for phosphoglycerate kinase 2.

125. The construct of claim 119, wherein said promoter is an oocyte-specific promoter.

126. A recombinant host cell, wherein said cell is transformed with any of the constructs of claims 120 through 125.

127. A composition comprising any of the constructs of claims 120 through 125 and a pharmaceutically acceptable carrier.

5 128. The composition of claim 127, wherein the pharmaceutically acceptable carrier is an adjuvant, solubilizer, stabilizer, diluent, anti-oxidant, liposome, micelle, or patch.

129. A device, comprising:

- a) a membrane suitable for implantation; and
- 10 b) the composition of claim 127 encapsulated within said membrane, wherein said membrane is permeable to the composition.

130. A device, comprising:

- a) a membrane suitable for implantation; and
- 15 b) the cells of claim 126 encapsulated within said membrane, wherein said cells secrete polypeptide, and wherein said membrane is impermeable to materials detrimental to said cells.

131. The selective binding agent of claims 17, 47, or 89 that is an antibody or a fragment thereof.

20 132. An antibody or fragment thereof that specifically binds SMC1 β polypeptide.

133. The antibody of claim 132 that is a monoclonal antibody.

134. A method according to claim 1 or claim 10 substantially as described and illustrated herein.

25 135. A compound as claimed in claim 68 or claim 70, substantially as herein described and illustrated.

136. Use of a compound of claim 135 in the manufacture of a medicament substantially as herein described and illustrated.

137. A compound for inducing the expression of a heterologous gene in a germ cell comprising an SMC1 β promoter comprising a sequence of SEQ ID NO: 12 or 13 operably linked to said heterologous gene.

138. A method of inducing expression of a heterologous gene in a germ cell comprising contacting said germ cell with an expression construct comprising said heterologous gene operably linked to an SMC1 β promoter comprising a sequence of SEQ ID NO: 12 or 13, under conditions effective to allow expression of said heterologous gene.